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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/825,692

04/16/2004

Peter Hotez

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EXAMINER

ZEMAN, ROBERT A

ART UNIT

PAPER NUMBER

1645

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
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3 MONTHS

02/20/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/825,692

Applicant(s)

HOTEZ ET AL.

Examiner

Robert A. Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 December 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 103 and 138-140 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 103 and 138-140 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment and response filed on 12-4-2006 are acknowledged. Claim 103 has been amended. Claims 34-36, 98-102 and 104-137 have been canceled. Claims 138-140 have been added. Claims 103 and 138-140 are pending and currently under examination.

Claim Rejections Withdrawn

The rejection of claims 103-109 and 135 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in light of the amendment thereto and in lieu of the written description rejection set forth below.

The rejection of claims 103-109 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions capable of stimulating an immune response in an animal *to* the antigen itself, does not reasonably provide enablement for immunogenic compositions capable of stimulating an immune response in an animal *to* hookworm is withdrawn in light of the amendment thereto and in lieu of the written description rejection set forth below.

The rejection of claims 103-104, 107-108 and 135 under 35 U.S.C. 102(a) as being anticipated by Pritchard (WO 01/62802 – IDS filed on 1-11-2005) is withdrawn in light of the amendment thereto.

The rejection of claims 103-104, 106 and 108 under 35 U.S.C. 102(b) as being anticipated by Bin et al. (Molecular and Biochemical Parasitology, 1999, Vol. 98, pages 143-149) is withdrawn in light of the amendment thereto.

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Claim Objections

Claim 103 is objected to because of the following informalities: The claim refers to “said mammal”. It is unclear what mammal applicant is referring to as there is no previous recitation of the limitation “mammal”. Appropriate correction is required.

New Grounds of Rejection

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 103 and newly added claims 138-140 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims are drawn to the use of immunological compositions (vaccines) comprising Na-ASP-2 and either *Na*-APR -1, *Na*-GST or *Na*-CP-2 to vaccinate against or elicit an immune response to a composition containing a hookworm antigen. In other words, the immune response generated is to a composition comprising **any** hookworm antigen. Moreover, the claimed method encompasses the induction of a protective immune response against “hookworm antigens”.

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The aforementioned claims are directed to encompass the hookworm antigens Na-ASP-2 and either Na- APR -1, Na-GST or Na-CP-2. Said designations do not satisfy the description requirement, as they are not linked to a specific protein sequence. Consequently, their recitation in the rejected claims are deemed to be laboratory designations with no specific sequence or structure associated with them

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The protein itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404. 1405 held that: "...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

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An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606. The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Claims 103 and 138-140 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use immunogenic compositions comprising *Na*-ASP-2 and either *Na*-APR-1, *Na*-GST or *Na*-CP-2 to elicit an immune response to *Na*-ASP-2 and either *Na*-APR-1, *Na*-GST or *Na*-CP-2, does not reasonably provide enablement for the use of said compositions to elicit an immune response to a composition comprising any other hookworm antigen nor their use for the induction of a protective immune response against any "hookworm antigen" or hookworm species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The rejected claims are drawn to the use of immunogenic compositions comprising *Na*-ASP-2 and either *Na*-APR-1, *Na*-GST or *Na*-CP-2 capable of stimulating an immune response (including a protective immune response) in an animal to any hookworm antigen. However, Applicant has failed to demonstrate that the administration of a composition comprising *Na*-

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ASP-2 and either *Na*-APR -1, *Na*-GST or *Na*-CP-2 would result in an immune response to any hookworm antigen other than those antigens that comprise the administered composition.

While the skill in the art of immunology is high, to date, prediction of a specific immune response for any given composition in any given animal is quite unpredictable. Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome **and form**

immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Additionally, as evidenced by Greenspan et al. (*Nature Biotechnology* 7: 936-937, 1999), defining epitopes is not as easy as it seems. Greenspan et al. recommends defining an epitope by the structural characterization of the molecular interface between the antigen and the antibody is necessary to define an "epitope" (page 937, column 2). According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Furthermore, an

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epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit an immune response to a given pathogen can only be identified empirically. This constitutes undue experimentation. Therefore, given the lack of success in the art, the lack of working examples commensurate in scope to the claimed invention and the unpredictability of the generation of directed immune responses, the specification, as filed, does not provide enablement for the use of compositions comprising *Na*-ASP-2 and either *Na*-APR -1, *Na*-GST or *Na*-CP-2 to elicit an immune response to a composition comprising any other hookworm antigen than those within the administered composition.

Moreover, the instant claims read on the prophylactic use of a composition comprising *Na*-ASP-2 and either *Na*-APR -1, *Na*-GST or *Na*-CP-2. To be a prophylactic composition, the composition must elicit protective immunity, demonstrable by pathogen challenge experiments in a reasonable model system. The specification, as filed, does not set forth that the claimed use of the claimed deletion provides any sort of protective immunity in any model system that can be extrapolated to humans or mammals. Additionally, the rejected claims read on vaccines against any and all hookworm species but the specification is silent as to what polypeptides would elicit a protective immune response against a given hookworm species. Even if one would expect a given polypeptide to elicit an immune response to hookworm, there is no way to predict whether said response would be protective. Hence, with regard to the use of "hookworm vaccines" comprising *Na*-ASP-2 and either *Na*-APR -1, *Na*-GST or *Na*-CP-2, the specification is not enabling.

Finally, the instant claims are drawn to "vaccinating" a mammal against a hookworm

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antigen. This is aspect of the claims are not enabled as "vaccination" by definition provides protection against a pathogen (i.e. an organism) or a disease.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 103 and 138-140 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 103 is rendered vague and indefinite by the use of the terms "*Na*-ASP-2, *Na*-APR-1, *Na*-GST and *Na*-CP-2". Said terms constitute laboratory designations engendering no specific sequence. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Claim 138 is rendered vague and indefinite by the use of the term "*Na*-APR-1". Said term constitutes a laboratory designation engendering no specific sequence. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

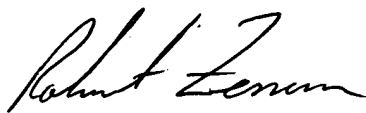
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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ROBERT A. ZEMAN
PRIMARY EXAMINER

February 12, 2007